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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,339	03/12/2004	Masahiro Kakehi	250307US0DIV	6720

22850 7590 04/04/2008

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ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
04/04/2008	ELECTRONIC

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/798,339
Filing Date: March 12, 2004
Appellant(s): KAKEHI ET AL.

James J. Kelly, PhD
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed January 28, 2008 appealing from the Office action mailed August 27, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Thaller et al. "Identification of the gene (*aphA*) encoding the class B acid phosphatase/phosphotransferase of *Escherichia coli* MG1655 and characterization of its product" FEMS Microbiology Letters, vol. 146 (1997), pages 191-198.

Cowman et al. "Molecular cloning of the gene (*ush*) from *Escherichia coli* specifying periplasmic UDP-sugar hydrolase (5'-nucleosidase)" Gene, vol. 12 (1980), pages 281-286.

Matsui et al. EP 1004 663 A1 (May 31, 2000) Process for producing purine nucleosides via fermentation.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thaller et al. alone or in view of Cowman et al.

Thaller et al. (form PTO-1449 filed March 12, 2004, reference AAB) teach the sequence of the *aphA* gene (page 193, Figure 1). They further characterize 5'-nucleotidase activity of the *E. coli* AphA enzyme (page 195, Table 1). They teach that another 5'-nucleotidase in *E. coli* is UshA (page 197, 2nd column, last paragraph). They suggest producing strains carrying aphA mutations (page 198).

Cowman et al. (form PTO-1449 filed March 12, 2004 , reference AAA) teach the ushA gene from *E. coli* encoding a 5'-nucleotidase.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce *E. coli* mutants having non-functional, for example, disrupted *ushA* gene and *aphA* gene. The motivation to produce such mutants is provided by Thaller et al. who teach 5'-nucleotide dephosphorylating activity of *ushA* gene and *aphA* gene. Mutants with disrupted *ushA* gene and *aphA* gene would have a higher yield of 5'-nucleotides. One of ordinary skill in the art at the time the invention was made would have a reasonable expectation of success because the structures of both *ushA* gene and *aphA* gene were known at the time the invention was made and methods for disrupting known genes were widely used.

Claims 9 and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thaller et al. alone or in view of Cowman et al. and further in view of Matsui et al.

The teachings of Thaller et al. and Cowman et al. are outlined above.

Matsui et al. (EP 1004 663 A1, form PTO-1449 filed March 12, 2004, reference AP) teach a method for producing purine nucleosides such as inosine and guanosine which are important as intermediate compounds for synthesis of 5'-inosinic acid and 5'-guanylic acid (page 2, [001], lines 5-7). They teach a microorganism which acquired the purine nucleoside-producing ability because of an increase of an activity of an enzyme involved in the purine nucleoside biosynthesis due to its gene overexpression (page 2, [0007]). They teach that enzyme can be PRPP amidotransferase that is desensitized (page 2, [0008]). They teach the mutation Lys326Glu in PRPP amidotransferase gene (*purF*) resulting in desensitizing the feedback inhibition (page 6, [0055]; page 10,

[0076])) and *E. coli* comprising said mutant PRPP amidotransferase (page 11). They further teach that in order to efficiently utilize the *purF* gene, it can be used with other genes involved in the IMP biosynthesis such as IMP dehydrogenase gene (*guaB*) and GMP synthetase gene (*guaA*) (page 7, [0064]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce *E. coli* mutants having non-functional, for example, disrupted *ushA* gene and *aphA* gene thus preventing the decomposition of inosine 5'-phosphate ester and guanosine 5'-phosphate ester and additional genes such as *purF*, *guaA* and *guaB* that increase their production. The motivation to produce such mutants is provided by Thaller et al. who teach 5'-nucleotide dephosphorylating activity of *ushA* gene and *aphA* gene and Matsui et al. who teach the role of *purF*, *guaA* and *guaB* in the nucleotide biosynthesis. One of ordinary skill in the art at the time the invention was made would have a reasonable expectation of success because the structures of all involved genes were known at the time the invention was made and methods for mutation of known genes were widely used.

(10) Response to Argument

Appellant argues "Thaller et al. describe the cloning of the *ushA* gene and the 5'-nucleotidase activity thereof. See the Abstract. There is no description that decreasing expression of the gene would lead to enhanced production of nucleoside 5'-phosphate esters. Cowman et al. identify the *aphA* gene and describe the dephosphorylation activity of that enzyme. See the Abstract and pages 195 and 196. In particular, the reference describes a hybrid plasmid encoding the enzyme. Cowman et al. explain at

page 285 of the reference that the plasmid may [be] useful in cloning applications. There is no teaching in the reference that decreasing expression of the gene would lead to enhanced production of nucleoside 5'-phosphate esters" (Brief, page 3).

Appellant further argues "Matsui et al. disclose a process for producing purine nucleosides via fermentation using a modified PRPP amidotransferase. See the Abstract. There is no teaching in the reference that decreasing expression of the *ushA* gene and *aphA* gene would lead to enhanced production of nucleoside 5'-phosphate esters. Thaller et al. alone or in combination with Cowman et al. and Matsui et al. fail to suggest the claimed method. Neither Thaller et al. or Cowman et al. suggest disrupting expression of the *ushA* and *aphA* genes, respectively, to for the purpose of preparing nucleoside 5'-phosphate esters" (Brief, page 4).

Therefore, Appellant concedes that both Thaller et al. and Cowman et al. identify *E. coli* enzymes that decompose nucleoside 5'-phosphate esters and that Matsui et al. teach that the modified PRPP amidotransferase increases the production of the same. As references used in a 103 not a 102 rejection, said references do not need to teach the very same invention, i.e. the claimed method for producing nucleoside 5'-phosphate ester. Said references only have to make the invention obvious. It is the position of the examiner that it would have been reasonable to expect that the elimination of enzymes (*aphA* and *ushA*) that decompose the product (nucleoside 5'-phosphate ester) and overexpression of enzymes (the modified PRPP amidotransferase) that lead to its increased production would be beneficial for the production of the product, i.e. to what the claimed method is aimed. No unexpected results have been shown or argued by

Appellant. The examiner's position is not contradictory to the Thaller et al. suggesting increasing expression of *aphA* as recited by Appellant on page 4. This is because it was suggested for the purposes of using the product that the claimed method is aimed to make. Thus, different ends would require different genetic manipulations of the gene such as its increased expression or lack of the expression.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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Conferees:

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